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FREE RADICALS AND CANCER

An additional electron spin resonance (ESR) signal at g = 2.005 has been observed in erythrocytes of patients with an acute lymphatic leukemia (ALL) and could be identified as the ascorbyl (SDA) radical. It will be produced by an interaction between ascorbic acid and copper containing proteins at cellular membrane levels. This interaction can occur only if a so-called masking substance is missing as in vitro experiments have shown. The SDA radical disappears again, that is the original ESR spectrum of healthy erythrocytes will be obtained, if ascorbate oxidase is added to ALL erythrocytes. In this case, like in model systems, SDA is oxidized further to dehydroascorbic acid followed by its degradation resulting finally in glyoxal.

ANTITUMOR THERAPIES BASED ON INHIBITION OF ANTIOXIDANT ENZYMES

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We have found in general that normal cells have substantial levels of the four primary antioxidant enzymes, copper and zinc containing superoxide dismutase (Cu-Zn SOD), manganese-containing superoxide dismutase (Mn SOD), catalase (CAT), and glutathione peroxidase (GP). In contrast, tumor cells in general have adequate levels of Cu-Zn SOD and GP, but diminished levels of Mn SOD and CAT. We have utilized this basic biochemical difference between normal cells and tumor cells to divise new antitumor therapies. In particular, we have found that if the remaining antioxidant enzymes of the tumor cell are inhibited (i.e., Cu-Zn SOD and GP), then the tumor cell is virtually defenseless against an oxidative insult, while the normal cell still has a functioning antioxidant defense system - namely Mn SOD and CAT. We will report that a particularly potent antitumor drug regimen is a combination of: 1) drugs that produce active oxygen - species such as adriamycin and bleomycin, 2) drugs that inhibit Cu-Zn SOD - such as diethyldithiocarbamate and D-penicillamine, and 3) drugs that inhibit GP.